# Community-dwelling men with dementia are at high risk of hip but not any other fracture: The Concord Health and Ageing in Men Project

Benjumin Hsu[1,2,3,4]*, Kerrin Bleicher[3]*, Louise M. Waite[3], Vasi Naganathan[3], Fiona M. Blyth[3], David J. Handelsman[2], David G. Le Couteur[2,3], Markus J. Seibel[2], Robert G. Cumming[2,3,4,5]

*joint first author

[1] Centre for Big Data Research in Health, UNSW Sydney, Sydney, New South Wales, Australia

[2] ANZAC Research Institute, University of Sydney and Concord Hospital, Sydney, New South Wales, Australia

[3] Centre for Education and Research on Ageing, University of Sydney and Concord Hospital, Sydney, New South Wales, Australia

[4] School of Public Health, University of Sydney, Sydney, New South Wales, Australia

[5] ARC Centre of Excellence in Population Ageing Research, University of Sydney, Sydney, New South Wales, Australia

Corresponding authors: Benjumin Hsu, Centre for Big Data Research in Health, UNSW Sydney, New South Wales, Australia 2052. E-mail: benjumin.hsu@unsw.edu.au

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**ABSTRACT**

**Aim:** The aim of this longitudinal study of older community-dwelling men was to examine the association between cognitive status at baseline, and falls, fractures, and bone loss over time.

**Method:** In the Concord Health and Ageing in Men Project, 1705 community-dwelling men aged 70 to 97 had detailed baseline clinical assessment of cognitive status (dementia, mild cognitive impairment (MCI) and normal cognition), as well as depression, physical activity, neuromuscular function, health status, sociodemographic, comorbidities, medication use and serum 25D, 1,25D and PTH levels. During a mean follow-up of 6-years, participants were contacted 4-monthly to ascertain incident falls and fractures, the latter being confirmed by radiographic reports. Bone mineral density (BMD) was measured by dual X-ray absorptiometry at multiple time-points.

**Results:** At baseline, 120 men were assessed to have MCI and 93 men to have dementia. Over time, there were 162 first incident fractures, including 43 hip and 32 vertebral fractures. In univariate models, baseline dementia but not MCI predicted increased incidence of hip fracture (HR:6.95, 95%CI:3.47-13.96) but not vertebral (HR:2.26, 95%CI:0.79-6.46) or non-hip-non-vertebral fracture (HR:0.73, 95%CI:0.27-1.99). The strong risk of hip fractures associated with dementia remained after accounting for potential confounders (HR:4.44, 95%CI:1.97-9.98). In multivariate analyses, dementia (IRR:2.26, 95%CI:1.70-2.99) but not MCI was associated with an increased risk of falls

compared with normal cognition. There was no associations between baseline dementia and change in BMD.

**Conclusions:** Older men with dementia, but not MCI, have a greater tendency to fall and sustain hip fractures but not any other types of fractures.

**Keywords:** bone loss; dementia; epidemiology; falls; fractures

## INTRODUCTION

Both dementia and hip fracture are strongly associated with substantial morbidity and adverse health outcomes, including an increased risk of mortality.(1, 2) Dementia complicates the acute management and care in people with hip fracture such as increasing hospital length of stay, time to rehabilitation and post fracture management.(3)

Several reports from different study populations have shown people with dementia and cognitive impairment have a higher prevalence and risk of hip fracture ((4-6) and see Supplementary references). However, these studies did not consider bone mineral density (BMD). Most studies only examined the relationship between dementia and fractures at the hip but not at other sites. To date, only two studies reported relationships between dementia and non-hip fractures.(4, 5) These studies were studies of patients hospitalized with fractures and relied entirely on hospital admission data which may not have correctly captured all dementia diagnoses or non-hip fractures. Furthermore, these two studies only accounted for age, sex and administrative records of comorbidities, and did not account for other important shared and intermediate risk factors.

The key aims of our longitudinal study of community-dwelling older men were to identify the relationship between baseline cognitive status and (a) different types of fractures (hip, vertebral and non-hip-non-vertebral) during 6-years, (b) falls during 2-years, and (c) change in BMD across 3 time-points during 5-years of follow-up.

## METHODS

### Study Participants

The Concord Health and Ageing in Men Project (CHAMP) is an epidemiological study of a wide range of health issues in older Australian men.(7) The selection of participants has been described in detail elsewhere.(7) Briefly, 1705 community-dwelling men aged 70 years and over participated at baseline (2005-07), 1367 returned for the 2-year follow-up (2007-09) and 958 for the 5-year follow-up (2012-13).

### Cognitive Status

At baseline, all participants were screened for cognitive status using the Mini Mental State Examination (MMSE) (8) and the short form Informant Questionnaire on Cognitive Decline (IQCODE).(9) Participants with a MMSE score less than 27 and/or IQCODE greater than 3.6 were invited to have a detailed clinical assessment by a study geriatrician.(10) The diagnosis for dementia, mild cognitive impairment (MCI) or normal cognition included a series of standardized review and assessment as described in detail elsewhere.(11) Diagnosis and classification of dementia was based on the Diagnostic and Statistical Manual of Mental Disorders (4th edition) revised criteria.(12) Participants deemed to have cognitive impairment but not dementia were given the diagnosis of MCI.(13)

**Fractures**

Following their baseline assessment, men were contacted by telephone every four months to ascertain incident fractures. If a fracture was reported, radiology reports were obtained either from the participant, or from hospital medical records and radiology practices. Only first incident fractures confirmed by radiographic reports were included. Pathological fractures and fractures of hands, fingers, feet, toes and the skull were excluded. All fractures that met the inclusion criteria were included regardless of trauma level.(14, 15) Fractures were categorized into three categories: hip, vertebral and non-hip-non-vertebral fracture. Time to censorship was either date of death, date of official withdrawal from the study or date of the last telephone contact. Participants have been follow-up for an average of 6 years.

**Falls**

At the four monthly follow-up phone calls, participants were asked whether they had fallen in the preceding 4 months and, if so, how many times they had fallen. Up to 2 years of telephone call cycles from baseline were used for this analysis. Falls data were categorized into 1 fall, 2 falls, and 3 or more falls. In addition to identifying the number of falls in 2 years, the number of falls prior to but not including the first fall-related fracture were also identified.

## Bone Mineral Density

BMD at the total hip and femoral neck, and lean mass was measured by dual X-ray absorptiometry (DXA) using a Hologic Discovery-W scanner (Hologic Inc., Bedford, MA, USA) at baseline, 2-year and 5-year follow-up. The same DXA scanner was used for all scans at the three assessments.

## Other Measurements

Baseline smoking status (never, ex-smoker, current), and the frequency and quantity of alcohol consumption per week, comorbidity, fracture history and general health status were based on self-report. Depressive symptoms were evaluated by the Geriatric Depression Scale, short form (GDS). Physical activity was measured by the Physical Activity Scale for the Elderly (PASE) questionnaire.

Height and weight were measured in the clinic and BMI was calculated as $kg/m^2$. Gait speed was measured at usual pace. A medication inventory was conducted by trained personnel during the baseline clinic visit. Trained staff used a stopwatch to record the time taken to walk 6 meters and narrow walk test, which required participants to keep their feet within two lines of tape 20 cm apart.(16) Sarcopenia was defined based on the European Working Group on Sarcopenia criteria of a low ALM/height ($<7.26$ $kg/m^2$) combined with low hand grip strength (<30 kg) and/or low

gait speed (≤0.8 m/s).(17) Fasting blood samples were collected from participants on the morning of their clinic visit. Serum 25 hydroxyvitamin D (25D), 1,25 dihydroxyvitamin D (1,25D) and parathyroid hormone (PTH) levels were measured by radioimmumoassay (RIA) using single-batch reagents (DiaSorin Inc., Stillwater, MN).

**Statistical Analysis**

The baseline descriptive characteristics of study participants by cognitive status (dementia, MCI, or normal) were generated and one-way analysis of variance (ANOVA) was performed to test the statistical difference between the three cognitive status groups.

The fall incidence rate ratios (IRR) were estimated using negative binomial regression analysis. This analysis enables adjustment for different follow-up times and the analysis of recurrent events that are not independent of one another.(18) The relative risks of fracture (hip, vertebral and non-hip-non-vertebral) were estimated using Cox proportional hazards regression models (hazard ratios, HR) and 95% confidence intervals. The association between cognitive status and change in BMD across three time-points was estimated using generalized estimating equations (GEE).(19) We conducted sensitivity analysis to ensure the fracture was not impacting on the falls model by excluding falls at the time of or after a fracture.

Models were initially unadjusted, then age adjusted and then multivariable adjusted. Age, comorbidity, general health status, smoking status, BMI, depression,

alcohol consumption, physical activity, serum 25D, 1,25D, PTH, psychoactive medications, osteoporosis medication, previous falls and fracture history, and BMD were tested for univariate associations with the relevant outcome of interest (falls or fractures). Only covariates which were statistically significant at ($p<0.05$) in univariate models were entered into the multivariate model: age, comorbidity, osteoporosis medications, GDS depression, physical activity and hip BMD.

The impact of incident falls, gait speed, inability to do a narrow walk and sarcopenia on fracture risk were added individually into the base multivariate fracture model. Similarly, to explore falls risk we added the following variables into a base multivariate falls model: inability to do a narrow walk and gait speed. Scores on these variables may be the result of dementia and their inclusion in the base model might mask other relationships. The inclusion of these respective variables was to explore whether these measurements might explain the observed relationships.

Interaction effects between dementia, covariates and time were tested in all models. Multicollinearity was assessed using the variance inflation factor with a threshold value of 10. Models were fit using SPSS software version 20 (IBM Corp., Armonk, NY, USA) and SAS software 9.3 (SAS Institute Inc., Cary, NC, USA).

**Ethics Approval**

All participants gave written informed consent. The study was approved by the Sydney South West Area Health Service Human Research Ethics Committee, Concord Repatriation General Hospital, Sydney, Australia.

## RESULTS

Of the 1705 CHAMP men, 164 men had unknown cognitive status because they had low scores on MMSE and high scores on IQCODE but were unable to be seen by the study geriatrician. These men were excluded from the final analyses resulting in 1541 men included in this study. Men with dementia tended to be older, have more comorbidities, have depression, lower BMD, poorer physical function and drink less alcohol than men with MCI or normal cognition (see Table 1).

Men with dementia were about four times more likely to have three or more falls during the first 2-year follow-up period compared with men with MCI and men with normal cognition (see Table 2). A greater proportion of men with dementia sustained a hip fracture, but there was a similar proportion of other fracture types in men with and without dementia (see Table 2).

The risk of any fall was greater for men with dementia than men with MCI or normal cognition (see Table 3). The unadjusted IRR for falls was 4.13 (95%CI: 3.22-5.29) for dementia and 1.09 (95%CI: 0.83-1.44) for MCI compared to normal cognition. Dementia remained associated with falls in both the age-adjusted (IRR: 4.33, 95%CI: 3.35-5.59) and multivariate-adjusted (IRR: 2.26, 95%CI: 1.70-2.99) models. The findings

were similar in sensitivity analyses which excluded falls at the time of and following any fracture (IRR: 3.27, 95%CI: 2.23-4.80) in the multivariate model (data not shown).

The greater risk for sustaining a hip fracture in men with dementia than men with MCI or normal cognition is detailed in Table 4 and Figure 1. In unadjusted models the risk of hip fracture was almost seven times greater (HR: 6.95, 95%CI: 3.47-13.96) and four times greater when adjusted for age (HR: 4.23, 95%CI: 2.00-8.93). Likewise, after accounting for potential confounders, the risk remained four times greater for men with dementia (HR: 4.44, 95%CI: 1.97-9.98). Inclusion of factors that are likely to be caused by dementia including any falls, slower gait speed and inability to do a narrow walk did not significantly attenuated the impact on the relationship between dementia and hip fractures. We further adjusted for sarcopenia in the base multivariate model and observed that sarcopenia did not further attenuate the relationship (data not shown). The findings were similar in sensitivity analyses which excluded falls following any fracture in the multivariate model (data not shown).

No associations were found between cognitive status and vertebral or non-hip-non-vertebral fracture in either unadjusted or multivariate-adjusted models. There were no interaction effects between dementia, covariates and time (data not shown). There were no longitudinal associations between cognitive status and BMD change. Neither dementia nor MCI were associated with baseline BMD or changes in BMD across three time-points over 5-years in either unadjusted or multivariate-adjusted models (data not shown).

## DISCUSSION

This is a longitudinal population-based study of community-dwelling older men which assesses the associations between cognitive status at baseline, and fractures, falls and change in BMD over time after accounting for a range of potential confounders, including BMD. Dementia conferred a two times greater risk of falling but a 4.8 times greater risk of a hip fracture after accounting for multiple potential confounders. However, there was no association between dementia and risk of other types of fractures nor between dementia and change in BMD. MCI did not increase either fracture risk or falls risk. Our findings suggest that older men with dementia may have a greater decline in motor function and impaired neurological reflexes during falls. The fact that there were no associations between dementia and non-hip fractures suggests that it may be the way older men with dementia fall that matters, particularly falls on the side which result in hip injuries.(20)

Only two studies have examined the relationship between dementia and non-hip fractures in older adults. Similar to our findings, the Taiwanese retrospective cohort study of 8,448 people aged 60 and over reported patients who visited ambulatory care centers or were hospitalized with a diagnosis of dementia were at greater risk of developing hip, but not wrist or vertebral fracture.(5) Likewise, an Australian study using hospital admission data reported people admitted with a fracture and a secondary diagnosis of dementia were more likely to have a hip fracture than a forearm, wrist or

hand fracture.(4) These two studies and the other studies examining dementia and hip fractures except for the recent UMEA 85+ study (6) were not population-based prospective cohort studies, but instead were retrospective registry-based studies, nested case-control studies, nested interventional studies, residential aged care studies or cross-sectional hospitalization data studies ((4, 5) and see Supplementary references).

Our findings in relations to falls are also consistent with a systematic review and meta-analysis showing dementia to be associated with risk of any falls and recurrent falls in community-dwelling older men.(21) The lack of observed associations between dementia and non-hip and non-hip-non-vertebral fractures in our study may be due to older men with dementia have a greater decline in motor function and impaired neurological reflexes during falls. Systematic reviews have reported that motor impairments such as impaired gait, muscular strength and balance are significant fall risk factors in older adults with cognitive impairments (22). These impairments may result in reduced opportunities for them to reach their hand or arm out during a fall. Men with normal cognition may have a better response to falls by trying to prevent further injuries with their upper or lower limbs, as oppose to older men with dementia who may simply land on their hips. The orientation of the fall most likely have the greatest impact on sustaining a hip fracture. We were unable to examine specifically whether men with dementia were more likely to have a backward fall resulting in rib or pelvis fracture.

It has been hypothesized that there may be common etiologies between dementia and osteoporosis which both have a similar epidemiology with marked increase in prevalence in older adults.(23) However, we did not find any associations between dementia and change in BMD over time, which suggests there may not be an independent link. Our finding suggest that dementia may not be associated with BMD loss but instead may be associated with decline in bone quality. The decline in bone quality is known to result in poor bone strength, which subsequently leads to sustaining hip fractures.(24) In addition, this finding suggests that medications used to increase or maintain bone density alone may not be sufficient to lower the risk of hip fractures in older men with dementia.

Falls prevention trials have been widely conducted in community-dwelling older people, however, dementia has been an exclusion criteria for almost all of the interventions.(25) A recent systematic review and meta-analysis of three randomized controlled trials has suggested that an exercise program may potentially prevent falls in older adults with dementia.(26) Our study suggests that falls prevention programs for older people with dementia should specifically target hip protection. Older men with dementia may have poor protective responses during a fall. The slow reaction times and speed of execution in conducting protective reactions may be the most problematic in older adults with dementia. Interventions for the prevention of falls-related injuries or hip protectors for preventing hip fractures have mainly focused on the cognitively intact older adults.(27, 28) Hence, well-designed randomized controlled trials on the use of hip

protectors, improving home safety by installing soft surface ground and individual tailored exercise program in older men and women with dementia are warranted.

A major strength of our study is that we included detailed clinical assessment of cognitive status at baseline which allowed us to make clinical diagnoses of dementia and MCI. We also confirmed all fractures using radiological reports. A further strength of CHAMP was that it includes a large and representative group of older Australian men, as demonstrated by similar socio-demographic and health characteristics in CHAMP men compared to older men in the nationally representative MATeS study (29).

However, we recorded 20% loss to follow-up from baseline to 2-year and a further 30% loss from 2-years to 5-years, which may have caused bias in our BMD analysis. However, loss to follow up in cohort studies of older people is inevitable because of the high mortality rate, which accounted for over a third of the loss in our cohort over 5-years. Although men were routinely contacted by telephone every four months to ascertain any incident, the possibility remains of underreporting and missing some fractures, particularly in those men with dementia. Furthermore, the small sample size in vertebral and non-hip-non-vertebral fractures occurred in men with dementia may suggest low statistical power. Finally, our study was limited to community-dwelling men and so may not apply to women.

In conclusion, older men with dementia, but not MCI, have an increased risk of falling and sustaining hip fractures but not any other types of fractures. Intervention

304 studies using innovative strategies are needed to prevent falls and falls-related hip
305 injuries in older men with dementia.

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307 **Disclosures**

308 The authors declare no conflict of interest.

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**TABLE 1. Characteristics of study participants (n=1541) according to diagnosed cognitive status at baseline (Mean (SD) or N (%))**

| | Normal (n=1328) | MCI (n=120) | Dementia (n=93) | p-value* |
|---|---|---|---|---|
| Age (yr) | 76.4 (5.1) | 77.3 (5.2) | 80.6 (5.9) | <0.001 |
| Body mass index (kg/m$^2$) | 27.8 (3.8) | 27.4 (3.8) | 26.9 (3.0) | 0.1 |
| Smoking | | | | |
| Previous smoker | 749 (56%) | 66 (55%) | 46 (50%) | 0.7 |
| Current smoker | 71 (5%) | 10 (8%) | 8 (9%) | |
| Alcohol (drinks/wk) | 9.1 (10.6) | 6.7 (8.9) | 6.7 (9.6) | 0.02 |
| Number of comorbidities | 2.5 (1.7) | 2.4 (1.7) | 3.0 (1.8) | 0.02 |
| Poor health status | 364 (28%) | 41 (35%) | 44 (49%) | <0.001 |
| GDS Depression | 142 (11%) | 22 (19%) | 38 (43%) | <0.001 |
| Psychoactive medication | 106 (8%) | 11 (9%) | 12 (13%) | 0.2 |
| Osteoporosis medication | 147 (11%) | 20 (17%) | 10 (11%) | 0.2 |
| Hip BMD (g/cm$^2$) | 0.94 (0.1) | 0.91 (0.1) | 0.92 (0.2) | 0.01 |
| Total BMD (g/cm$^2$) | 1.04 (0.1) | 1.02 (0.1) | 1.02 (0.1) | 0.1 |
| Previous fracture history | 604 (46%) | 37 (31%) | 36 (39%) | 0.004 |
| Vitamin 25D (nmol/L) | 56.9 (22.4) | 57.2 (21.8) | 54.1 (23.4) | 0.5 |
| Vitamin 1,25D (pmol/L) | 111.1 (65.6) | 113.7 (74.1) | 103.2 (63.1) | 0.1 |
| PTH (pg/ml) | 6.1 (2.9) | 5.9 (2.3) | 5.8 (3.3) | 0.7 |
| Physical Activity Scale for the Elderly (PASE) | 130.7 (60.0) | 126.9 (60.0) | 95.8 (54.1) | <0.001 |
| Gait speed (m/s) | 0.90 (0.2) | 0.84 (0.2) | 0.69 (0.2) | <0.001 |
| Unable narrow walk | 347 (26%) | 34 (29%) | 46 (51%) | <0.001 |

*p-value: ANOVA for continuous variables and chi-square test for categorical variables

**TABLE 2. Total falls over 2-years and incident fracture over 6-years follow-up according to baseline cognitive status (N (%))**

| | Normal (n=1328) | MCI (n=120) | Dementia (n=93) |
|---|---|---|---|
| Falls | | | |
| 1 | 194 (15%) | 21 (18%) | 14 (15%) |
| 2 | 85 (6%) | 6 (5%) | 4 (4%) |
| 3+ | 76 (6%) | 10 (8%) | 22 (24%) |
| Fractures | | | |
| Hip | 29 (2%) | 3 (3%) | 11 (12%) |
| Vertebral | 26 (2%) | 2 (2%) | 4 (4%) |
| Non-hip Non-vertebral | 77 (6%) | 7 (6%) | 4 (4%) |

**TABLE 3. Incident rate ratios (95%CI) of falls over 2-years follow-up based on baseline cognitive status**

| | Unadjusted | Age-adjusted | Multivariate* | Multivariate + narrow walk | Multivariate + gait speed |
|---|---|---|---|---|---|
| Normal | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| MCI | 1.09 (0.83-1.44) | 1.07 (0.80-1.43) | 1.09 (0.80-1.47) | 1.03 (0.76-1.42) | 0.76 (0.53-1.07) |
| Dementia | 4.13 (3.22-5.29) | 4.33 (3.35-5.59) | 2.26 (1.70-2.99) | 2.13 (1.59-2.84) | 1.59 (1.15-2.19) |

*multivariate model adjusted for age, number of comorbidities, osteoporosis medications, GDS depression and Physical Activity Scale for the Elderly (PASE)

**TABLE 4. Hazard ratio (95% CI) for associations between baseline cognitive status and fractures over an average of 6-year follow-up**

| | Unadjusted | Multivariate* | Multivariate + falls | Multivariate + narrow walk | Multivariate + gait speed |
|---|---|---|---|---|---|
| Hip | | | | | |
| Normal | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| MCI | 1.17 (0.36-3.83) | 0.91 (0.28-3.00) | 0.92 (0.28-3.05) | 1.01 (0.31-3.33) | 1.08 (0.32-3.61) |
| Dementia | 6.95 (3.47-13.96) | 4.44 (1.97-9.98) | 4.38 (1.93-9.94) | 5.23 (2.33-11.73) | 5.64 (2.36-13.48) |
| Vertebral | | | | | |
| Normal | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| MCI | 0.85 (0.20-3.60) | 0.81 (0.19-3.46) | 0.78 (0.18-3.32) | 0.88 (0.21-3.75) | 0.93 (0.22-4.00) |
| Dementia | 2.26 (0.79-6.46) | 1.74 (0.56-5.44) | 1.79 (0.56-5.72) | 1.33 (0.37-4.82) | 2.11 (0.66-6.75) |
| Non-hip Non-vertebral | | | | | |
| Normal | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| MCI | 1.01 (0.46-2.18) | 0.79 (0.34-1.81) | 0.77 (0.33-1.77) | 0.67 (0.27-1.66) | 0.72 (0.29-1.79) |
| Dementia | 0.73 (0.27-1.99) | 0.52 (0.16-1.71) | 0.47 (0.14-1.56) | 0.56 (0.17-1.85) | 0.65 (0.20-2.16) |

*multivariate model adjusted for age, number of comorbidities, osteoporosis medications, GDS depression, Physical Activity Scale for the Elderly (PASE) and hip BMD

†the age-adjusted results for hip fractures are shown in text

FIGURE 1. Cumulative hazard rates of hip, vertebral and non-hip non-vertebral fracture according to baseline diagnosed cognitive status (dementia, MCI or normal)